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Noninvasive detection of silent coronary artery disease in patients with essential hypertension, alone or associated with type 2 diabetes mellitus, using dipyridamole stress 99mtechnetium-sestamibi myocardial perfusion imaging.

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Abstract

BACKGROUND: Coronary artery disease (CAD) is the leading cause of morbidity and mortality in hypertensive and diabetic patients. Early diagnosis of CAD and identification of high-risk subgroups, followed by appropriate therapy, may therefore enhance survival.

OBJECTIVES: To prospectively establish the prevalence of silent CAD in asymptomatic patients with essential hypertension (EH), and to establish to what extent type 2 diabetes mellitus (DM) modifies the prevalence and severity of silent CAD in these patients.

METHODS: The study population consisted of 543 patients 45 years of age and older with EH (n=321) or EH with type 2 DM (n=222), without typical angina or known CAD, selected according to criteria defined by the American Diabetes Association. All patients underwent dipyridamole stress and rest 99mtechnetium sestamibi myocardial single-photon emission computed tomography imaging. The stress and rest myocardial images were divided into 20 segments and blindly scored by two experienced observers. The summed stress score and summed rest score were obtained by adding the scores of the 20 segments of the stress and rest sestamibi images, respectively. The difference between the summed stress score and the summed rest score was defined as the summed difference score, representing reversible ischemia.

RESULTS: There was a significant difference (P=0.001) between the percentage of EH patients with (41.4%) and without (27.7%) DM, with regard to abnormal summed stress scores. Moreover, hypertensive, diabetic patients had a significantly greater incidence of moderate to severe ischemia (P=0.011). In addition, a significantly greater proportion of hypertensive patients with DM showed reversible ischemia compared with EH patients without DM (39.6% versus 24.6%; P<0.0001). Proteinuria and dyspnea were significant predictors of silent ischemia in EH patients with DM.

CONCLUSIONS: In this high-risk population screened according to the American Diabetes Association criteria with dipyridamole sestamibi myocardial single-photon emission computed tomography imaging, the prevalence of silent ischemia was 28% in EH patients. It is noteworthy that the prevalence (41%) and severity of silent ischemia were significantly greater in EH patients with DM.

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PROGNOSTIC IMPLICATIONS OF ECHOCARDIOGRAPHICALLY DETERMINED LEFT VENTRICULAR MASS IN THE FRAMINGHAM HEART STUDY

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Abstract A pattern of left ventricular hypertrophy evident on the electrocardiogram is a harbinger of morbidity and mortality from cardiovascular disease. Echocardiography permits the noninvasive determination of left ventricular mass and the examination of its role as a precursor of morbidity and mortality. We examined the relation of left ventricular mass to the incidence of cardiovascular disease, mortality from cardiovascular disease, and mortality from all causes in 3220 subjects enrolled in the Framingham Heart Study who were 40 years of age or older and free of clinically apparent cardiovascular disease, in whom left ventricular mass was determined echocardiographically.

During a four-year follow-up period, there were 208 incident cardiovascular events, 37 deaths from cardiovascular disease, and 124 deaths from all causes. Left ventricular mass, determined echocardiographically, was associated with all outcome events. This relation persisted after we adjusted for age, diastolic blood pressure, pulse pressure, treatment for hypertension, cigarette smoking, diabetes, obesity, the ratio of total cholesterol to high-density lipoprotein cholesterol, and electrocardiographic evidence of left ventricular hypertrophy. In men, the risk factor–adjusted relative risk of cardiovascular disease was 1.49 for each increment of 50 g per meter in left ventricular mass corrected for the subject's height (95 percent confidence interval, 1.20 to 1.85); in women, it was 1.57 (95 percent confidence interval, 1.20 to 2.04). Left ventricular mass (corrected for height) was also associated with the incidence of death from cardiovascular disease (relative risk, 1.73 [95 percent confidence interval, 1.19 to 2.52] in men and 2.12 [95 percent confidence interval, 1.28 to 3.49] in women). Left ventricular mass (corrected for height) was associated with death from all causes (relative risk, 1.49 [95 percent confidence interval, 1.14 to 1.94] in men and 2.01 [95 percent confidence interval, 1.44 to 2.81] in women).

We conclude that the estimation of left ventricular mass by echocardiography offers prognostic information beyond that provided by the evaluation of traditional cardiovascular risk factors. An increase in left ventricular mass predicts a higher incidence of clinical events, including death, attributable to cardiovascular disease. (N Engl J Med 1990; 322:1561-6.)

LEFT ventricular hypertrophy, although infrequently noted on the electrocardiogram, imparts a substantial risk of morbidity and mortality.[1-3] Echocardiography has permitted the reliable, noninvasive estimation of left ventricular mass[4-7] and has proved a more sensitive tool for the detection of left ventricular hypertrophy than other techniques previously available. The Framingham Heart Study has developed sex-specific criteria for left ventricular hypertrophy, based on the distribution of left ventricular mass in a healthy reference population.[8] The application of these criteria to a large, free-living population studied with echocardiography has documented a prevalence of left ventricular hypertrophy of 15 to 20 percent in adults[9]; this value is considerably higher than the prevalence of electrocardiographically demonstrated left ventricular hypertrophy in the same population.[10]

Recent reports have documented an increased risk of the sequelae of cardiovascular disease in subjects with echocardiographic evidence of left ventricular hypertrophy.[11-14] In a study of more than 1000 elderly men and women, we found an association between echocardiographically determined left ventricular mass and the incidence of coronary heart disease; this association persisted after adjustment for traditional cardiac risk factors.[14] The present investigation was undertaken to extend this smaller study by examining the relation of left ventricular mass, determined echocardiographically, to the four-year risk of cardiovascular disease, mortality from cardiovascular disease, and mortality from all causes in a much larger group of middle-aged and elderly subjects enrolled in the Framingham Heart Study.

From the Framingham Heart Study, Framingham, Mass., and the Division of Epidemiology and Clinical Applications of the National Heart, Lung, and Blood Institute, Bethesda, Md. (D.L., R.J.G., W.P.C.), the National Center for Health Statistics, Hyattsville, Md. (D.D.S.); and the Department of Medicine and the Section of Preventive Medicine and Epidemiology, Boston University School of Medicine, Boston (W.B.K.). Address reprint requests to Dr. Levy at the Framingham Heart Study, 5 Thurber St., Framingham, MA 01701.

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METHODS

Study Population

In 1948, residents of Framingham, Massachusetts, who were between the ages of 28 and 62 were enrolled in a prospective epidemiologic study. The selection criteria and study design have been described previously.[15,16] In 1971, children of the original study population and the spouses of those children were enrolled in the Framingham Offspring Study.[17] From 1979 to 1983, the surviving members of the original cohort underwent their 16th biennial examination and subjects in the Offspring Study underwent their second examination; these examinations routinely included 12-lead resting electrocardiography, measurements of resting blood pressure, anthropometric measurements, determinations of blood glucose levels, and echocardiography. Electrocardiograms were examined for evidence of definite left ventricular hypertrophy (increased voltage plus a "strain" pattern).[1] Diabetes was indicated by any one of the following: a fasting blood glucose level ≥7.77 mmol per liter (140 mg per deciliter), a random nonfasting blood glucose level ≥11.11 mmol per liter (200 mg per deciliter), or the use of insulin or an oral hypoglycemic agent. Data regarding cigarette smoking and measurements of plasma total cholesterol and high-density lipoprotein cholesterol were obtained from the 15th biennial examination of the members of the original cohort and the second examination of subjects in the Offspring Study (index examination).

Outcome Events

To be eligible for inclusion in this study, subjects in the Offspring Study and members of the original study cohort had to be free of clinically apparent cardiovascular disease. Because of the low incidence of morbidity and mortality from cardiovascular disease in

Journal of Cardiovascular Magnetic Resonance

RESEARCH Open Access

Evaluation of diastolic function by three-dimensional volume tracking of the mitral annulus with cardiovascular magnetic resonance: comparison with tissue Doppler imaging

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Abstract

Background: Measurement of mitral annulus (MA) dynamics is an important component of the evaluation of left ventricular (LV) diastolic function; MA velocities are commonly measured using tissue Doppler imaging (TDI). This study aimed to examine the clinical potential of a semi-automated cardiovascular magnetic resonance (CMR) technique for quantifying global LV diastolic function, using 3D volume tracking of the MA with conventional cine-CMR images.

Methods: 124 consecutive patients with normal ejection fraction underwent both clinically indicated transthoracic echocardiography (TTE) and CMR within 2 months. Interpolated 3D reconstruction of the MA over time was performed with semi-automated atrioventricular junction (AVJ) tracking in long-axis cine-CMR images, producing an MA sweep volume over the cardiac cycle. CMR-based diastolic function was evaluated, using the following parameters: peak volume sweep rates in early diastole (PSR_E) and atrial systole (PSR_A), PSR_E/PSR_A ratio, deceleration time of sweep volume (DT_{SV}), and 50% diastolic sweep volume recovery time ($DSVRT_{50}$); these were compared with TTE diastolic measurements.

Results: Patients with TTE-based diastolic dysfunction (n = 62) showed significantly different normalized MA sweep volume profiles compared to those with TTE-based normal diastolic function (n = 62), including a lower PSR_E ($5.25 \pm 1.38\ s^{-1}$ vs. $7.72 \pm 1.7\ s^{-1}$), a higher PSR_A ($6.56 \pm 1.99\ s^{-1}$ vs. $4.67 \pm 1.38\ s^{-1}$), a lower PSR_E/PSR_A ratio (0.9 ± 0.44 vs. 1.82 ± 0.69), a longer DT_{SV} (144 ± 55 ms vs. 96 ± 37 ms), and a longer $DSVRT_{50}$ ($25.0 \pm 11.0\%$ vs. $15.6 \pm 4.0\%$) (all $p < 0.05$). CMR diastolic parameters were independent predictors of TTE-based diastolic dysfunction after adjusting for left ventricular hypertrophy, hypertension, and coronary artery disease. Good correlations were observed between CMR PSR_E/PSR_A and early-to-late diastolic annular velocity ratios (e'/a') measured by TDI ($r = 0.756$ to 0.828, $p < 0.001$).

Conclusions: 3D MA sweep volumes generated by semi-automated AVJ tracking in routinely acquired CMR images yielded diastolic parameters that were effective in identifying patients with diastolic dysfunction when correlated with TTE-based variables.

Keywords: Diastolic function, Mitral annulus, Cardiovascular magnetic resonance, Echocardiography, Feature-tracking

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Comparison of 99mTc tetrofosmin gated SPECT measurements of left ventricular volumes and ejection fraction with MRI over a wide range of values.

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Abstract

The calculation of ejection fraction using gated single photon emission computed tomography (SPECT) has been widely validated against a range of other techniques. There have been fewer studies validating left ventricular volumes. We compared quantitative gated SPECT (QGS) with magnetic resonance imaging (MRI) measurements of left ventricular ejection fraction and end diastolic volume in 50 patients with a large range of ventricular dimensions. MRI data were obtained using a turbo gradient echo pulse sequence (TGE) in 17 patients and a steady state free precession pulse sequence (SSFP) in 33 patients. There was good correlation between ejection fraction and end diastolic volume measurements from SPECT and MRI (r=0.82, r=0.90, respectively) but the mean SPECT values were significantly lower (ejection fraction, 6.6+/-6.4% points; end diastolic volume, 18.4+/-25.4 ml) than those obtained from MRI. Bland-Altman analysis showed some large differences in individual patients but no trends in the data either in ejection fraction over a range from 15% to 70% or in end diastolic volume, range 75-400 ml. SSFP gave a larger difference for end diastolic volume measurement compared to SPECT than did TGE, although this difference did not reach significance. Both SSFP and TGE gave similar values for the difference between MRI and SPECT for the measurement of ejection fraction. We suggest that the difference in EF may be a result of 8 frames being used for gating in QGS but 12-18 for MR. Differences in volumes may be related to the different spatial resolution and the exclusion or inclusion of trabeculation and papillary muscles between SPECT and MRI. Differences between SSFP and TGE may be caused by differing delineation of the endocardial border, dependent on the particular acquisition sequence. In conclusion, QGS values correlated well with MRI, but a correction factor may be needed if direct comparison is made.

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Repeatability of left ventricular ejection fraction and volume measurement for 99mTc-tetrofosmin gated single photon emission computed tomography (SPECT).

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Abstract

OBJECTIVES: This study was carried out to assess the repeatability of left ventricular ejection fraction (EF) and volume values obtained using Cedars-Sinai quantitative gated single photon emission computed tomography (SPECT) (QGS) software and relatively low doses of 400-600 MBq of 99mTc-tetrofosmin.

METHODS: Repeatability was assessed in a group of 75 patients, with both normal and reduced EF, who underwent repeat 99mTc-tetrofosmin gated SPECT studies and showed no clinical change in cardiac status. Gated SPECT data were acquired 1 h after injection at rest of 400-600 MBq of 99mTc-tetrofosmin. The standard patient dose was 400 MBq; however, some patients with a weight of >90 kg were given increased doses up to a maximum of 600 MBq.

RESULTS: There was good correlation of EF and volumes between the first and repeat measurements, and no significant difference between the mean EF and volumes for both the initial and repeat measurements. Background-corrected counts in the left ventricle were calculated and patients were divided into two groups: one with low counts and one with high counts. The mean difference in EF between the first and repeat measurements was significantly higher for patients in the low count group compared with those in the high count group, but there was no significant change in volume. Similarly, the mean sequential difference in EF was significantly higher for patients with normal EF, but there was no significant difference in volume.

CONCLUSIONS: We have demonstrated that EF measured using 99mTc-tetrofosmin gated SPECT is repeatable, particularly for patients with low EF, provided that adequate left ventricular counts are obtained. This will require doses greater than 400 MBq in larger patients. Ventricular volumes calculated using QGS may not be sufficiently repeatable for clinical use.

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Direct Evidence of Impaired Cardiac Sympathetic Innervation in Essential Hypertensive Patients with Left Ventricular Hypertrophy

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Increased sympathetic nervous activity has been proposed as one of the causes of left ventricular hypertrophy (LVH) associated with hypertension. However, the precise relationship is not fully understood. **Methods:** To elucidate the relationship between myocardial sympathetic nervous activity and LVH in patients with essential hypertension (EHT), we performed ^{123}I-metaiodobenzylguanidine (MIBG) myocardial scintigraphy in 49 patients with EHT and 17 normotensive control subjects. Sympathetic innervation of the left ventricle was evaluated using SPECT, and the whole heart uptake of the tracer was quantitatively assessed as the heart-to-mediastinum uptake ratio on both the early (15-min) and delayed (5-hr) images. Myocardial washout rate (MWR) of the tracer from 15 min to 5 hr after the isotope administration was also calculated. The left ventricular mass index (LVMI) was determined echocardiographically. **Results:** In 49 hypertensive patients, there was a negative correlation between LVMI and heart-to-mediastinum uptake ratio on both the early and delayed images ($r = -0.55$, $p < 0.0001$; $r = -0.63$, $p < 0.0001$, respectively). In addition, there was a positive correlation between the LVMI and MWR of ^{123}I-MIBG in these hypertensive patients ($r = 0.59$, $p < 0.0001$). As for the regional uptake of the tracer, there was no significant difference between control subjects and hypertensive patients without cardiac hypertrophy, but a significant decrease of the uptake in the inferior and lateral regions was observed in hypertensive patients with cardiac hypertrophy. **Conclusion:** Patients with EHT had decreased accumulation and increased MWR of ^{123}I-MIBG in proportion to the degree of LVH. Hypertensive patients with cardiac hypertrophy had impaired sympathetic innervation in the inferior and lateral regions of the left ventricle.

Key Words: sympathetic nervous system; norepinephrine; left ventricular hypertrophy; iodine radioisotope; hypertension

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Essential hypertension (EHT) is a major risk factor for the progression of cardiovascular damage in such organs as the brain, heart and kidney. Left ventricular hypertrophy (LVH), one of the types of end-organ damage associated with hypertension, is recognized as an independent risk factor for cardiovascular events (*1*), including cardiac sudden death (*2*). It is recognized that not only mechanical factors, but also humoral factors, are related to LVH in hypertension. Increased sympathetic nervous activity has been proposed as one of the influential factors on LVH (*3–5*), based on the observations that catecholamine administration induces LVH (*3*) and that sympatholytic intervention diminishes myocardial hypertrophy (*4*). In addition, alpha-1 adrenergic agonists were found to be potent stimuli for the hypertrophy of fetal cardiac myocytes (*5*). However, some experimental studies reported that chemical or surgical sympathectomy failed to block the development of LVH induced by hypoxia or hypertension (*6,7*). Moreover, Cooper et al. (*8*) postulated that mechanical load itself, rather than catecholamines, was directly responsible for cardiac hypertrophy. Thus, the role of sympathetic nervous activity in the genesis of LVH, especially in humans, has not been fully elucidated.

Iodine-123-labeled metaiodobenzylguanidine (MIBG) is a norepinephrine analog that is taken up by sympathetic nerve

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Myocardial imaging with 123I-metaiodobenzylguanidine in essential hypertension and renovascular hypertension.

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Abstract

Iodine-123 metaiodobenzylguanidine (MIBG) myocardial imaging is considered to reflect cardiac sympathetic function. We performed myocardial MIBG scintigraphy and echocardiography in 27 patients with essential hypertension (EHT), 7 patients with renovascular hypertension (RVHT), and 8 normotensive subjects (NT) to investigate alterations in MIBG myocardial imaging in the presence of hypertension and left ventricular hypertrophy (LVH). EHT were divided into two groups based on LV wall thickness; EHT with LVH group (> or = 13 mm, n = 15) and EHT without LVH group (< 13 mm, n = 12). The delayed uptake of MIBG was decreased, and the washout rate of MIBG was greater in the EHT with LVH group than EHT without LVH group or NT group. The washout rate was correlated with LV mass and LV diastolic function (as assessed by mitral flow). In RVHT group, the MIBG washout rate increased even without LVH, compared with NT and EHT without LVH groups. In summary, the washout rate of MIBG increased in parallel with the development of LVH in EHT and increased independently of the LV mass in RVHT. Cardiac sympathetic function could be altered in hypertensive LVH and in renovascular hypertension.

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